REMARKS

Claims 1-3, 7, 177-192 and 194-196 have been canceled without prejudice as being directed to non-elected subject matter. Claims 4-6, 8-176, 193-198 and 199-206 are pending.

The abstract has been amended to specifically recite the structure shown in Formula IV. Support for this amendment may be found, for example, in the specification as filed at page 15. Claims 4, 5, 8, 9, 26, 27, 30, 31, 32, 37, 38, 40, 42, 44, 46, 48, 50, 59, 62, 63, 161 and 169 have been amended to more clearly define the subject matter of the present invention, to correct typographical errors and to exclude non-elected subject matter. Claims 38, 40, 42, 46 and 48 have also been converted from dependent to independent format.

New claims 199-201 and 207, 210 and 211 have been added to specifically recite pharmaceutical compositions and packages comprising the compounds in claims 4 and 27. Support for these claims may be found, for example, in the specification at pages 34, and 47-51. Support for these claims is also found in original claims 180, 181, and 183. These latter claims are believed to have been inadvertently included in the non-elected group since they clearly fall within the scope of Group IV.

New claims 202-203 and 208-209 recite specific functional properties for the compounds of claims 4 and 27. Support for

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these claims may be found, for example, in the specification at page 36.

New claims 204, 205 and 206 recite the subject matter of canceled claims 24, 86 and 87, respectively, as independent claims. No new matter is added by any of the amendments herein.

The Examiner noted that the references listed on PTO form 1449 (Paper No. 5) are missing. Applicants submit copies of these references herewith, and request that the Examiner initial this PTO form 1449.

The Examiner is of the view that the abstract should contain a chemical structure. Applicants have amended the abstract to specifically recite Formula IV, and Applicants believe that this objection has been overcome.

Claims 4-6, 8, 30, 31 and 32-37 stand rejected under 35 U.S.C. §102(b) as being anticipated by Cho et al. (WO 98/00402). The Examiner is of the view that Cho et al. teaches the general preparation of piperazine derivatives in which a phenyl is linked to one piperazine nitrogen and a phenyl or pyridyl is attached to the other piperazine nitrogen via a carbonyl- or thiocarbonyl-containing linker. More specifically, the Examiner believes that certain compounds described by Cho et al. fall within the scope of the present claims.

Applicants respectfully traverse the rejection base on Cho et al. Cho et al. is directed to piperazine derivatives having

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antitumor activity. The ring corresponding to Ar_2 of the claimed invention is phenyl, and the ring corresponding to Ar_1 of the claimed invention is substituted with a group ("Z") that is always *ortho* to the point of attachment and is limited in scope. Cho et al. does not teach or suggest compounds in which Ar_2 comprises a heteroatom, or in which Z is not present, and Cho et al. does not teach or suggest the use of such compounds as capsaicin receptor antagonists. Applicants have amended claims 4 and 31 to exclude compounds in which Ar_2 is phenyl. In claims 8 and 32, phenyl is not among the possible Ar_2 groups, and Applicants believe that no amendment of claims 8 and 32 is needed. Claims 27 and 30 have been amended to exclude compounds in which R_5 is hydroxyl, lower alkyl, lower alkoxy, piperazine, pyridyl or thienyl. Applicants submit that the rejection based on Cho et al. has been overcome.

Claims 4-6, 27, 28 and 32 stand rejected under 35 U.S.C. §102(b) as being anticipated by Bock et al. (U.S. Patent No. 5,756,504). In particular, the Examiner is of the view that Bock et al. teaches the synthesis of 1-(2,4-dimethoxyphenylacetyl)-4-(2-methylphenyl)piperazine. Applicants respectfully traverse this ground for rejection. Bock et al. is directed to oxytocin receptor antagonists, and does not teach or suggest compounds of the claimed invention. Applicants have amended claims 4 and 27 to exclude CR_BR_B' from the list of

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possible A moieties. Claim 32 already recites that A is NH or O, and Applicants submit that no amendment of claim 32 is necessary. Applicants submit that the rejection based on Bock et al. has been overcome.

Claims 4-6 stand rejected under 35 U.S.C. §102(b) as being anticipated by Kulagowski et al. (U.S. Patent No. 5,792,768). In particular, the Examiner asserts that Kulagowski et al. teaches the synthesis of 1-(2-benzimidazol-2-yl)acetyl-4-phenylpiperazine. Applicants respectfully traverse this rejection. Kulagowski et al. is directed to antipsychotic benzimidazole derivatives. The compounds recited therein contain a $-CH_2-$ moiety at the position corresponding to A recited in the claims. As noted above, Applicants have amended claim 4 to exclude CR_BR_B' from the list of possible A moieties. Kulagowski et al. does not teach or suggest compounds in which A is one of the moieties recited within claim 4, as amended. Applicants submit that the rejection based on Kulagowski has been obviated.

Claims 4-6, 8-30, 31, 32-176 and 193-198 stand rejected under 35 USC §112, second paragraph, as being indefinite. In particular, the Examiner is of the view that the term "heterocycloalkyl" is not clear. Applicants respectfully traverse this rejection. Applicants believe the definition of this term in the specification at page 45 is clear. Those

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skilled in the art would understand heterocycloalkyl, in view of the definition in the specification, to mean a cyclic system consisting of carbon atoms and at least one hetero atom, and where the heterocycloalkyl group is bound to the parent group by any of the ring members, unless otherwise specified. Nonetheless, to facilitate allowance, Applicants have amended claims 4, 5, 8, 9, 27, 31, 32 and 50 to replace the term "heterocycloalkyl" with "heterocycle," as suggested by the Examiner. Applicants request that this rejection be withdrawn.

Claims 194-196, directed to the manufacture of a medicament, have been canceled.

Finally, the Examiner is of the view that the phrase "the compound or salt is not addictive" in claim 193 is not clear. Applicants respectfully traverse this ground for rejection. The term "addictive" is well known in the art and is understood to refer to compounds that result in substance dependence when administered to a patient in a therapeutically effective amount. Criteria for establishing substance dependence are very specific, and are recited in, for example, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (American Psychiatric Association, 2000) pages 192-198, a copy of which is submitted herewith. Applicants believe that this ground for rejection has been overcome.

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Applicants enclose herewith copies of the references cited in the PTO Form 1449 submitted previously.

Allowance of the elected claims is respectfully solicited. If the Examiner believes that discussion of the application will be helpful, the Examiner is encouraged to contact the undersigned attorney.

Respectfully submitted,

Dated: February 7, 2003 By: _____

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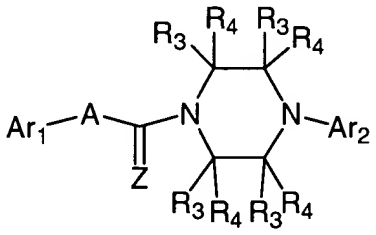
Version with Markings to Show Changes Made

In the Abstract:

Disclosed are diaryl piperazines and related compounds of the following formula



wherein the variables are as defined in the specification. These compounds are selective modulators of capsaicin receptors, including human capsaicin receptors, that are, therefore, useful in the treatment of a chronic and acute pain conditions, itch and urinary incontinence. Methods of treatment of such disorders and well as packaged pharmaceutical compositions are also provided. Compounds of the invention are also useful as probes for the localization of capsaicin receptors and as standards in assays for capsaicin receptor binding and capsaicin receptor mediated cation conductance. Methods of using the compounds in receptor localization studies are given.

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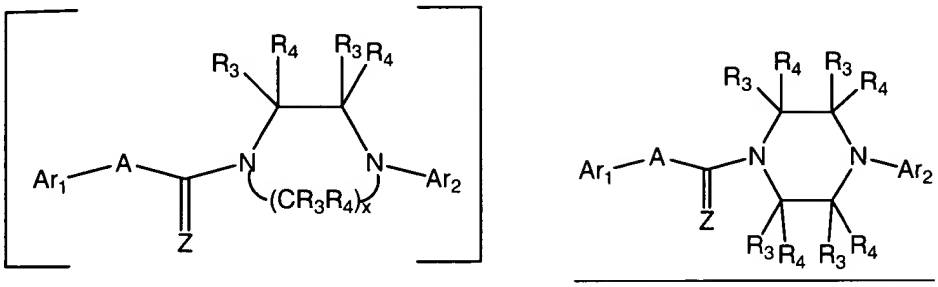
In the Claims:

4. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, [CR_BR_B',] $NR_ACR_BR_B'$, CR_B $R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and alkyl;

Z is oxygen or sulfur;

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO[,]; optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio;

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optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -$S(O)_nNH$alkyl; optionally substituted -$S(O)_nN$(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted -$NHS(O)_n$alkyl; optionally substituted -$NS(O)_n$(alkyl)(alkyl); optionally substituted saturated or partially unsaturated [heterocycloalkyl] heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated [heterocycloalkyl] heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be joined] to form an optionally substituted aryl ring, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted, or a saturated, partially

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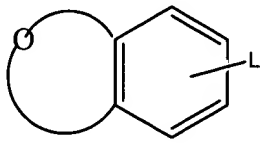
unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

Ar_1 [and Ar_2 may be the same or different and are] is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; [or] and

(b) [Ar_1 and Ar_2 may be the same or different and represent a] bicyclic oxygen-containing [group] groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8

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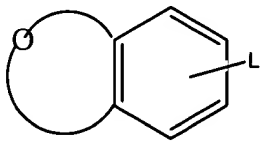
ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

Ar_2 is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; and

(b) bicyclic oxygen-containing groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of halogen, [cyano,] nitro, halo(C_{1-6})alkyl,

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halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy [substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, -XR_7,] and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, [-NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),] -S(O)$_n$(C_{1-4}alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl$_1$)(C_{1-4}alkyl$_2$) where alkyl$_1$ and alkyl$_2$ may be joined to form a [heterocycloalkyl ring] <u>heterocycle</u> of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms <u>independently</u> selected from N, O, and S, -XR_7, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_8-, -O-, -S(O)$_n$-, -NH-, -NR_8-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR_8-, -S(O)$_n$NH-, -S(O)$_n$$NR_8$-, NHC(=O)-, -$NR_8$C(=O)-, -NHS(O)$_n$-, and -$NR_8$S(O)$_n$-;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or

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one or more double or triple bonds, each of which 1 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), $-NHS(O)_n(alkyl)$, $-S(O)_n(alkyl)$, $-S(O)_nNH(alkyl)$, $-S(O)_nN(alkyl_3)(alkyl_4)$ where $alkyl_3$ and $alkyl_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

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n is independently chosen at each occurrence from 0, 1, and 2 [;

and

x is 1 or 3].

5. (Amended) A compound or salt according to Claim 4, wherein:

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and C_{1-6}alkyl;

each R_3 and R_4 [are] is independently

(a) chosen [at each occurrence] from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6,

-N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6,

$-XR_7$, and Y; or

(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be joined] to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of

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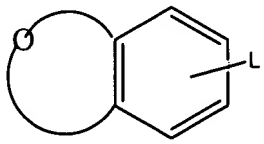
from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

[Ar_1 and Ar_2 may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; or

Ar_1 and Ar_2 may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8

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ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, and C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), $-S(O)_n(C_{1-4}$alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl$_1$)(C_{1-4}alkyl$_2$) where alkyl$_1$ and alkyl$_2$ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, -C(=O)-, -C(=O)O-, -C(=O)NH-, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, NHC(=O)-, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;]

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups,

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and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(C_{1-4}alkyl), -N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl), -NHS(O)$_n$(C_{1-4}alkyl), -S(O)$_n$(C_{1-4}alkyl), -S(O)$_n$NH(C_{1-4}alkyl),

-S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y'; and

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which [may be further] are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

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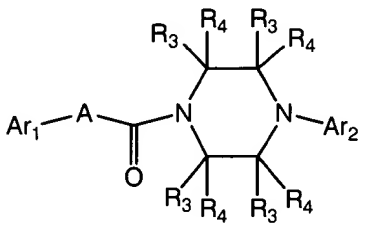
wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S [;

n is independently chosen at each occurrence from 0, 1, and 2; and

x is 1 or 3].

8. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen or alkyl;

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted

alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -$S(O)_nNH$alkyl; optionally substituted -$S(O)_nN$(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted -$NHS(O)_n$alkyl; optionally substituted -$NS(O)_n$(alkyl)(alkyl); optionally substituted saturated or partially unsaturated [heterocycloalkyl] <u>heterocycle</u> of from 5 to 8 atoms, which saturated or partially unsaturated [heterocycloalkyl] <u>heterocycle</u> contains 1, 2, or 3 heteroatoms <u>independently</u> selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring <u>independently</u> selected from the group consisting of N, O, and S; or

(b) [any two] <u>joined to a</u> R_3 [and] <u>or</u> R_4 not attached to the same carbon [may be joined] to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially

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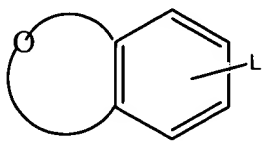
unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

Ar_1 and Ar_2 [may be the same or different and] are independently selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl; wherein Ar_1 is optionally mono-, di-, or trisubstituted with R_5, and Ar_2 is optionally mono-, di-, or trisubstituted with R_9; [or] and

(b) [Ar_1 and Ar_2 may be the same or different and represent a] bicyclic oxygen-containing [group] groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on

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the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6, alkenyl substituted with 0-2 R_6, alkynyl substituted with 0-2 R_6, alkoxy [substituted with 0-2 R_6, -NH(alkyl) substituted with 0-2 R_6, -N(alkyl)(alkyl) where each alkyl is independently substituted with 0-2 R_6, $-XR_7$,] and Y;

R_9 is independently selected at each occurrence from the group consisting of [cyano,] nitro, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6, alkenyl substituted with 0-2 R_6, alkynyl substituted with 0-2 R_6, alkoxy substituted with 0-2 R_6, [-NH(alkyl) substituted with 0-2 R_6, -N(alkyl)(alkyl) where each alkyl is independently substituted with 0-2 R_6, $-XR_7$,] and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, [-NH(alkyl), -N(alkyl)(alkyl),] $-S(O)_n$(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON($alkyl_1$)($alkyl_2$) where $alkyl_1$ and $alkyl_2$ may be joined to form a [heterocycloalkyl ring] heterocycle of from 5 to 8 ring

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atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), $-NHS(O)_n$(alkyl), $-S(O)_n$(alkyl), $-S(O)_nNH$(alkyl), $-S(O)_nN(alkyl_3)(alkyl_4)$ where $alkyl_3$ and $alkyl_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

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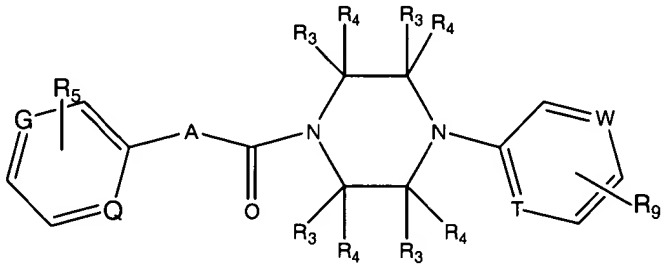
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which [may be further] <u>are unsubstituted or</u> substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to [8-memberered] <u>8-membered</u> heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

9. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and are selected from the group consisting of N, CH, and CR_5, wherein T or W or both is N;

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where

B

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and alkyl;

Z is oxygen or sulfur;

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted C_{1-6}alkyl; optionally substituted C_{2-6}alkenyl; optionally substituted C_{2-6}alkynyl; optionally substituted C_{1-6}alkoxy; optionally substituted mono or di(C_{1-6})alkylamino; optionally substituted C_{1-6}alkylthio; optionally substituted C_{1-6}alkyl ketone; optionally substituted C_{1-6}alkylester; optionally substituted C_{1-6}alkylsulfinyl; optionally substituted C_{1-6}alkylsulfonyl; optionally substituted mono- or di(C_{1-6})alkylcarboxamide; optionally substituted -$S(O)_n$NH C_{1-6}alkyl; optionally substituted -$S(O)_n$N(C_{1-6}alkyl)(C_{1-6}alkyl); optionally substituted -NHC(=O) C_{1-6}alkyl; optionally substituted -NC(=O)(C_{1-6}alkyl)(C_{1-6}alkyl); optionally substituted -NHS$(O)_n$$C_{1-6}$alkyl; optionally substituted -NS$(O)_n$(C_{1-6}alkyl)(C_{1-6}alkyl); optionally substituted saturated or partially unsaturated [heterocycloalkyl] heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated [heterocycloalkyl] heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

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optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be joined] to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 represents 1 to 3 substituents [and is] independently selected at each occurrence from the group consisting of cyano, hydroxy, amino, C_{3-6} alkyl substituted with 0-2 R_6, C_{2-6} alkenyl substituted with 0-2 R_6, C_{2-6} alkynyl substituted with 0-2 R_6, C_{3-6} alkoxy [substituted with 0-2 R_6], $-NH(C_{1-6}alkyl)$ substituted with 0-2 R_6, $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ where each alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y;

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R_9 represents 0 to 3 substituents [and is] independently selected at each occurrence from the group consisting of halogen, [cyano,] nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, [-NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$,] and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, [-NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),] $-S(O)_n(C_{1-4}alkyl)$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON($C_{1-4}alkyl_1$)($C_{1-4}alkyl_2$) where $alkyl_1$ and $alkyl_2$ may be joined to form a [heterocycloalkyl ring] <u>heterocycle</u> of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms <u>independently</u> selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, -C(=O)-, -C(=O)O-, -C(=O)NH-, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, NHC(=O)-, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups,

B

and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -NHC(O)(C_{1-4}alkyl), -N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl), -NHS(O)$_n$(C_{1-4}alkyl), -S(O)$_n$(C_{1-4}alkyl), -S(O)$_n$NH(C_{1-4}alkyl), -S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

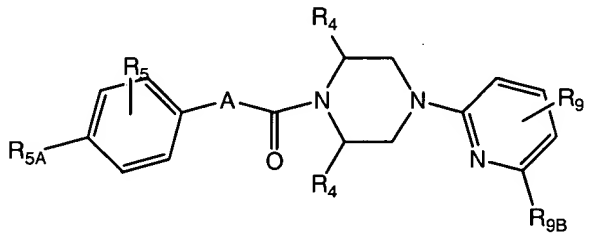
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which [may be further] are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

B

wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

26. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH_2NH;

R_4 is independently chosen from hydrogen and C_{1-4} alkyl;

R_5 represents 0 to 2 substituents [and is] independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy [substituted with 0-2 R_6], -NH(C_{1-6}alkyl) substituted with 0-2 R_6, and -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6;

R_9 represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen,

B

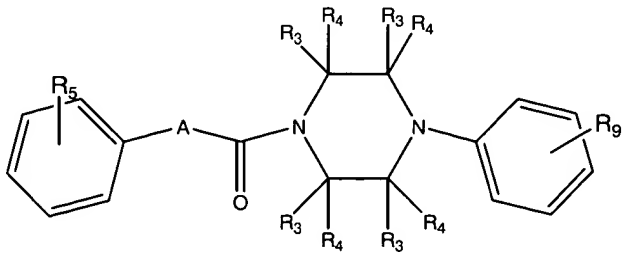
[cyano,] nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, and C_{1-6}alkoxy substituted with 0-2 R_6 [, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, and -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6];

R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6} alkoxy, -NH(C_{1-6} alkyl), and -N(C_{1-6} alkyl)(C_{1-6} alkyl);

R_{9B} is independently selected from the group consisting of halogen, nitro, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl, and C_{1-6} alkoxy [, -NH(C_{1-6} alkyl), and -N(C_{1-6} alkyl)(C_{1-6} alkyl)]; and

R_6 is independently selected at each occurrence the group consisting of halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4} alkyl), and -N(C_{1-4} alkyl)(C_{1-4} alkyl).

27. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of a single bond, S, NR_A, [CHR_B,] NR_ACHR_B, CHR_BNR_A, $-CR_A=CR_B-$, and C_3H_4; where R_A and R_B are independently selected at each occurrence from the group consisting of hydrogen and alkyl;

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNH$alkyl; optionally substituted $-S(O)_nN$(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted $-NHS(O)_n$alkyl; optionally substituted $-NS(O)_n$(alkyl)(alkyl); optionally substituted saturated or partially unsaturated [heterocycloalkyl] heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated [heterocycloalkyl] heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

B

optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be joined] to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 [is] represents 0-3 substituents independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, [C_{1-6} alkyl substituted with 0-2 R_6,] C_{2-6} alkenyl substituted with 0-2 R_6, and C_{2-6} alkynyl substituted with 0-2 R_6 [,C_{1-6} alkoxy substituted with 0-2 R_6, -NH(C_{1-6} alkyl) substituted with 0-2 R_6, -N(C_{1-6} alkyl)(C_{1-6} alkyl) where each alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y];

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R_9 represents 0-3 substituents [and is] independently selected at each occurrence from the group consisting of bromo, haloalkyl, haloalkoxy, hydroxy, C_{2-6} alkyl substituted with 0-2 R_6, C_{2-6} alkenyl substituted with 0-2 R_6, C_{2-6} alkynyl substituted with 0-2 R_6, and C_{2-6} alkoxy [substituted with 0-2 R_6, -NH(C_{2-6} alkyl) substituted with 0-2 R_6, -N(C_{2-6} alkyl)(C_{2-6} alkyl) where each C_{2-6} alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y];

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, [-NH(alkyl), -N(alkyl)(alkyl),] $-S(O)_n$(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON($alkyl_1$)($alkyl_2$) where $alkyl_1$ and $alkyl_2$ may be joined to form a [heterocycloalkyl ring] heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, -C(=O)-, -C(=O)O-, -C(=O)NH-, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, NHC(=O)-, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups

B

consisting of 3 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 3 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -$NHS(O)_n$(alkyl), -$S(O)_n$(alkyl), -$S(O)_nNH$(alkyl), -$S(O)_nN(alkyl_3)(alkyl_4)$ where $alkyl_3$ and $alkyl_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which [may be further] are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

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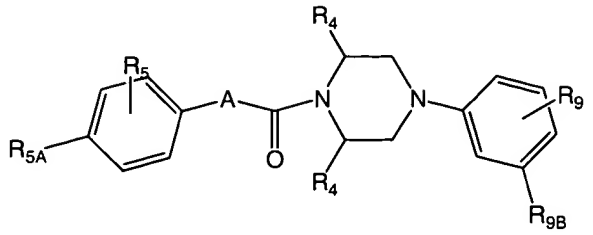
30. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH_2NH;

R_4 is independently selected at each occurrence from hydrogen and C_{1-4}alkyl;

R_5 represents 0 to 2 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, [hydroxy,] amino, [C_{1-6}alkyl substituted with 0-2 R_6,] C_{2-6}alkenyl substituted with 0-2 R_6, and C_{2-6}alkynyl substituted with 0-2 R_6 [, C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, and -N(C_{1-6}alkyl)(C_{1-6}alkyl), where each C_{1-6}alkyl is independently substituted with 0-2 R_6];

R_9 represents 0 to 2 substituents and is independently selected at each occurrence from the group consisting of halogen, [cyano,] nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6,

B

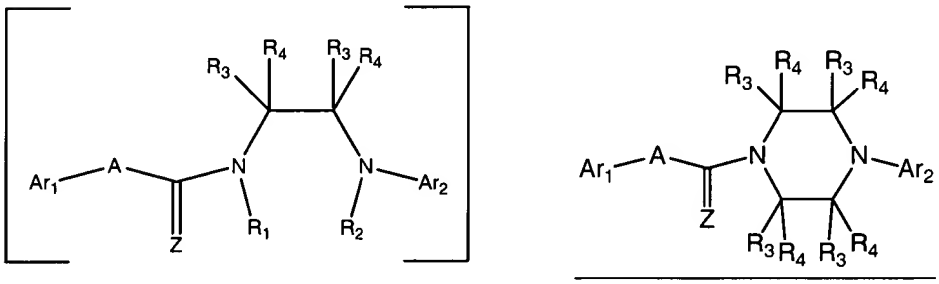
and C_{1-6}alkoxy substituted with 0-2 R_6 [, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, and -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6];

R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6} alkoxy, -NH(C_{1-6} alkyl), and -N(C_{1-6} alkyl)(C_1-C_6 alkyl);

R_{9B} is independently selected from the group consisting of trifluoromethoxy, hydroxy, C_{2-6} alkyl, and C_{2-6} alkoxy [, -NH(C_{2-6} alkyl), and -N(C_{2-6} alkyl)(C_{2-6} alkyl)]; and

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, C_{1-4} alkyl, and C_{1-4} alkoxy [, -NH(C_{1-4} alkyl), and -N(C_{1-4} alkyl)(C_{1-4} alkyl)].

31. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein the compound or pharmaceutically acceptable salt thereof exhibits an EC50 or K_i of 1 micromolar or less in a standard

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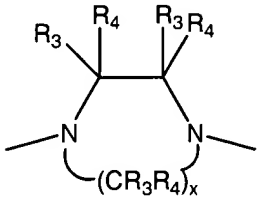
assay of capsaicin receptor mediated calcium mobilization; and wherein

A is absent or is selected from the group consisting of O, S, NR_A, [CR_BR_B',] $NR_ACR_BR_B'$, CR_B $R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and C_{1-6} alkyl;

Z is oxygen or sulfur;

[R_1 and R_2 independently represent hydrogen or C_{1-6} alkyl; or R_1 and R_2 are taken together to form a 5 to 8 membered nitrogen-containing ring of the formula:



wherein x is 1, 2, or 3;]

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, $-NH(C_{1-6}$alkyl) substituted with 0-2 R_6, $-N(C_{1-6}$alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y; or

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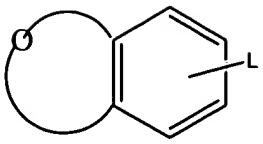
(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be are joined] to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

Ar_1 [and Ar_2 may be the same or different and are] is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; [or] and

(b) [Ar_1 and Ar_2 may be the same or different and represent a] bicyclic oxygen-containing [group] groups of the formula:

B

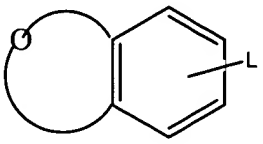


optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

Ar_2 is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; and

(b) bicyclic oxygen-containing groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on

B

the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of halogen, [cyano,] nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy [substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$], and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, [-NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),] -S(O)$_n$(C_{1-4}alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl$_1$)(C_{1-4}alkyl$_2$) where alkyl$_1$ and alkyl$_2$ may be joined to form a [heterocycloalkyl ring] heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, -S(O)$_n$-, -NH-, $-NR_8-$, -

B

C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR_8-, -S(O)$_n$NH-, -S(O)$_n$$NR_8$-, NHC(=O)-, -$NR_8$C(=O)-, -NHS(O)$_n$-, and -$NR_8$S(O)$_n$-;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -NHC(O)(C_{1-4}alkyl), -N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl), -NHS(O)$_n$(C_{1-4}alkyl), -S(O)$_n$(C_{1-4}alkyl), -S(O)$_n$NH(C_{1-4}alkyl), -S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

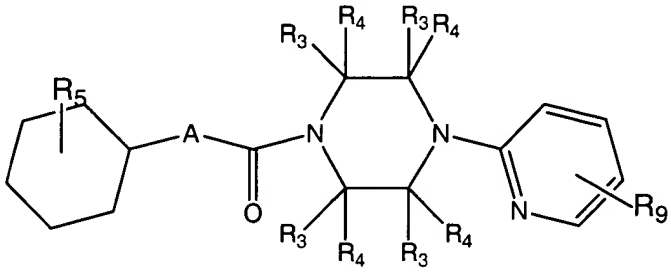
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano,

C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

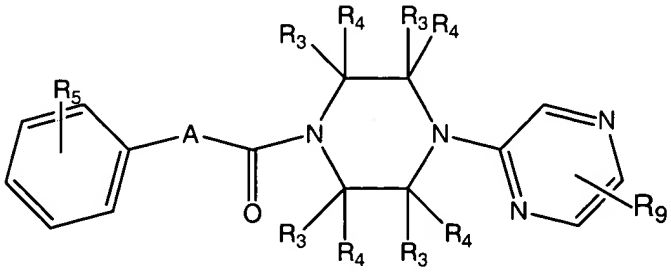
wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

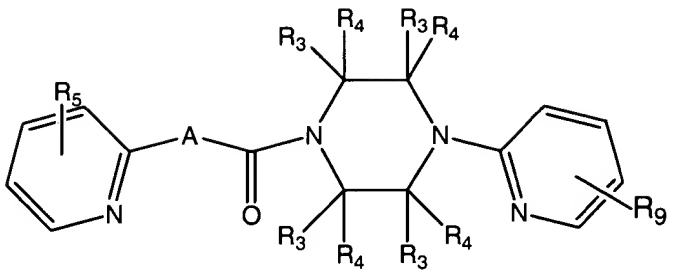
32. (Amended) A compound of the Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F:



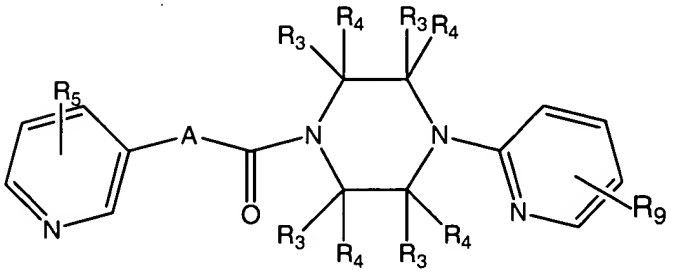
Formula A



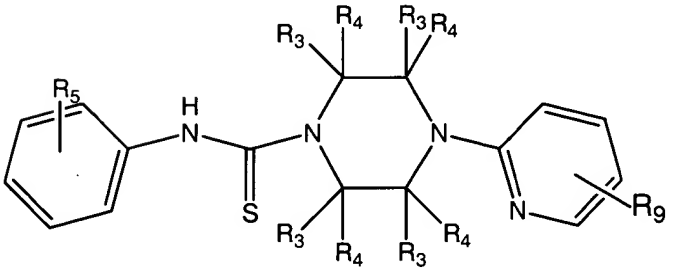
Formula B



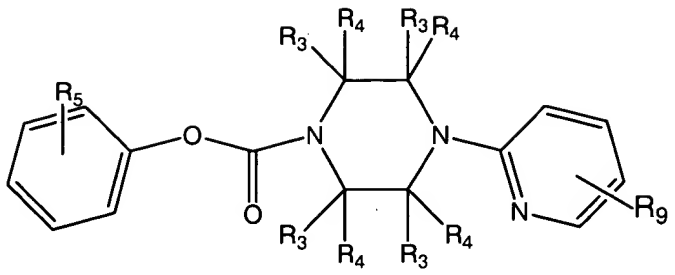
Formula C



Formula D



Formula E



Formula F

or a pharmaceutically acceptable salt of Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F, wherein

A represents NH or O;

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y; or

(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be joined] to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of

B

from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 [and R_9 each represent] represents from 1 to 3 substituents [and are] independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy [substituted with 0-2 R_6], -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y;

R_9 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, [-NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),] $-S(O)_n(C_{1-4}$alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl$_1$)(C_{1-4}alkyl$_2$) where alkyl$_1$ and alkyl$_2$ may be joined to form a [heterocycloalkyl ring] heterocycle

B

of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms [may be further] is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-NHC(O)(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-4}alkyl)$, $-S(O)_nNH(C_{1-4}alkyl)$, $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$ where $C_{1-4}alkyl_3$ and $C_{1-4}alkyl_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

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Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

37. (Amended) A compound or salt according to Claim 32, wherein:

A represents NH;

R_3 represents hydrogen;

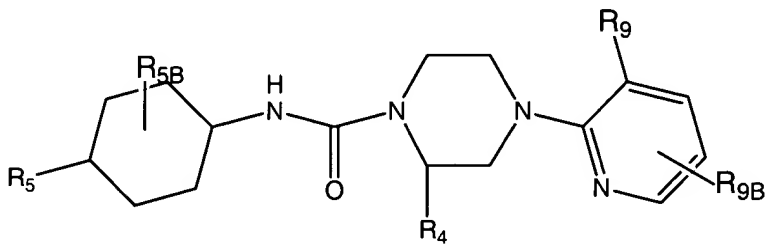
R_4 is independently chosen at each occurrence from hydrogen and methyl; and

R_5 [and R_9 each represent] represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

B

R_9 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, and C_{3-8} cycloalkyl.

38. (Amended) A compound or salt [according to Claim 37] of the Formula A-1



Formula A-1

wherein

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent [up] from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy,

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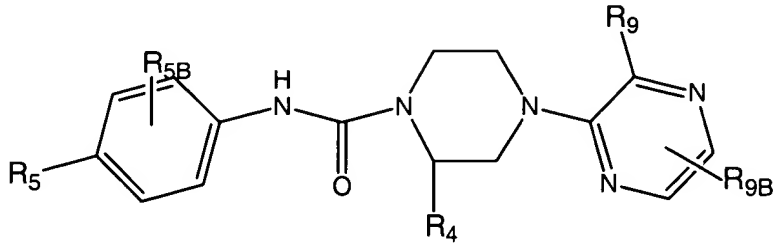
hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

40. (Amended) A compound or salt [according to Claim 37] of Formula B-1



Formula B-1

wherein

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent [up] from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

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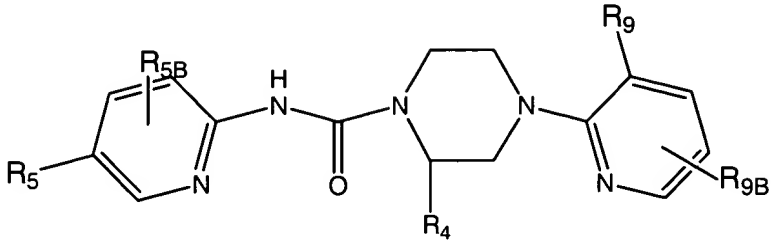
42. (Amended) A compound or salt [according to Claim 37] of Formula C-1[:]



Formula C-1

wherein:

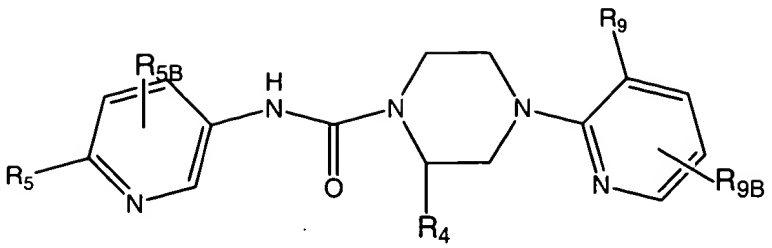
R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent [up] from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

44. (Amended) A compound or salt according to Claim 37 of Formula D-1

B



Formula D-1

wherein:

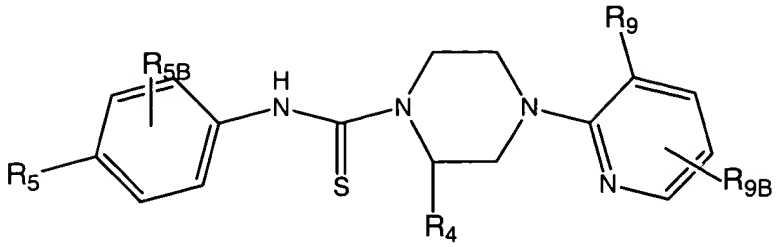
R_5 [and R_9 are independently] is selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl;

R_9 is selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent [up] from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

46. (Amended) A compound or salt [according to Claim 37,] of Formula E-1

B



Formula E-1

wherein:

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent [up] from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

48. (Amended) A compound of salt [according to Claim 37] of Formula F-1

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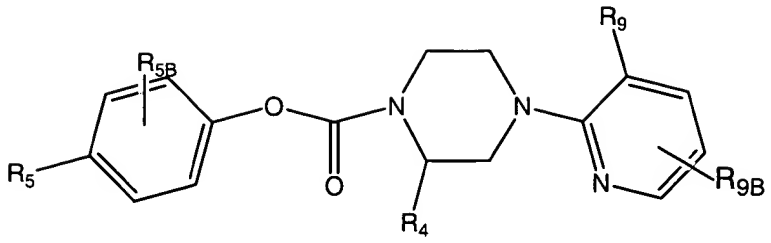


Formula F-1

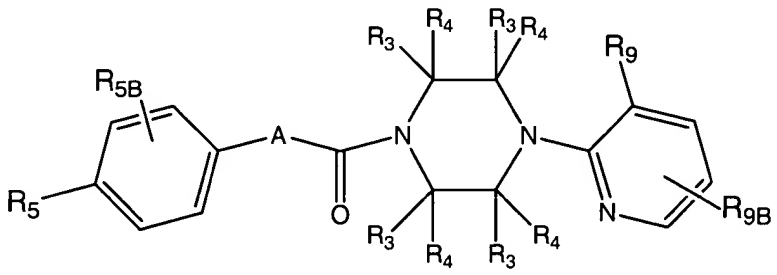
wherein:

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, [-NH(C_{1-6}alkyl] -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent [up] from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

50. (Amended) A compound of the Formula:



B

or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and C_{1-6} alkyl;

each R_3 and R_4 [are] is independently

(a) selected [at each occurrence] from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, $-NH(C_{1-6}alkyl)$ substituted with 0-2 R_6, $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y; or

(b) [any two] joined to a R_3 [and] or R_4 not attached to the same carbon [may be joined] to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

B

R_5 is selected from the group consisting of bromo, fluoro, iodo, halo(C_{1-6})alkyl, halo(C_{3-6})alkoxy, C_{3-6}alkyl substituted with 0-3 R_6, C_{2-6}alkenyl substituted with 0-3 R_6, C_{2-6}alkynyl substituted with 0-3 R_6, C_{3-6}alkoxy [substituted with 0-2 R_6], (C_{3-8}cycloalkyl)C_{1-4}alkyl, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is substituted with 0-2 R_6, Y, -(C=O)Y, -(CH_2)Y, and -(CH(CN))Y;

R_9 is selected from the group consisting of halogen, cyano, -N(SO_2C_{1-6}alkyl)(SO_2C_{1-6}alkyl),-SO_2NH_2, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, and C_{1-6}alkoxy substituted with 0-2 R_6 [, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is substituted with 0-2 R_6];

R_{5B} [and R_{9B} each represent] represents from 0 to 2 substituents [and are] independently selected at each occurrence from the group consisting of

(a) halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, (C_{3-8}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy [substituted with 0-2 R_6], -NH(C_{1-6}alkyl) substituted with 0-2 R_6, [and] -N(C_{1-6}alkyl)(C_{1-6}alkyl) where

B

each C_{1-6}alkyl is independently substituted with 0-2 R_6, and Y; and [any two R_5 and R_{5B} bound to adjacent atoms may be]

(b) groups that are joined to R_5 to form a C_{3-8}cycloalkyl group or a [heterocycloalkyl group] saturated or partially unsaturated heterocycle, each of which is optionally substituted by from 1 to 5 substituents independently chosen from cyano, halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), halo(C_{1-4})alkyl, and halo(C_{1-4})alkoxy, wherein the [heterocycloalkyl group] saturated or partially unsaturated heterocycle [consists of] contains from 4 to 8 ring atoms [and contains] of which 1, 2, or 3 are heteroatoms independently selected from N, O, and S;

R_{9B} represents from 0 to 2 substituents independently selected at each occurrence from halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, (C_{3-8}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, and Y;

R_6 is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, [-NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),] -S(O)$_n$(C_{1-4}alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl$_1$)(C_{1-4}alkyl$_2$) where alkyl$_1$ and alkyl$_2$

may be joined to form a [heterocycloalkyl ring] heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}alkyl)$, $NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-NHC(O)(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-4}alkyl)$, $-S(O)_nNH(C_{1-4}alkyl)$, $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$ where $C_{1-4}alkyl_3$ and $C_{1-4}alkyl_4$ [may be] are optionally joined to form a [heterocycloalkyl ring] heterocycle consisting of from 5 to 8 ring atoms and

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containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

wherein said 3- to [8-memberered] 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

59. (Amended) A compound or salt according to Claim 58 wherein:

R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-3})alkyl, and C_{1-3}alkoxy [, -NH(C_{1-3}alkyl), and -N(C_{1-3}alkyl)(C_{1-3}alkyl)].

62. (Amended) A compound or salt according to Claim 57, wherein:

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R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-3})alkyl, and C_{1-3}alkoxy [, -NH(C_{1-3}alkyl), and -N(C_{1-3}alkyl)(C_{1-3}alkyl)];

R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy; and

R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, [and] C_{1-2}alkyl, and C_{1-2}alkoxy.

63. (Amended) A compound or salt according to Claim 57, wherein:

R_5 is selected from the group consisting of bromo, fluoro, iodo, halo(C_{1-6})alkyl, halo(C_{3-6})alkoxy, C_{3-6}alkyl substituted with 0-3 R_6, C_{2-6}alkenyl substituted with 0-3 R_6, Y, -(C=O)Y, -(CH_2)Y, and -(CH(CN))Y;

R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-2})alkyl, and C_{1-3}alkoxy [, -NH(C_{1-6}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl)];

R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy; and

R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, [and] C_{1-2}alkyl, and C_{1-2}alkoxy.

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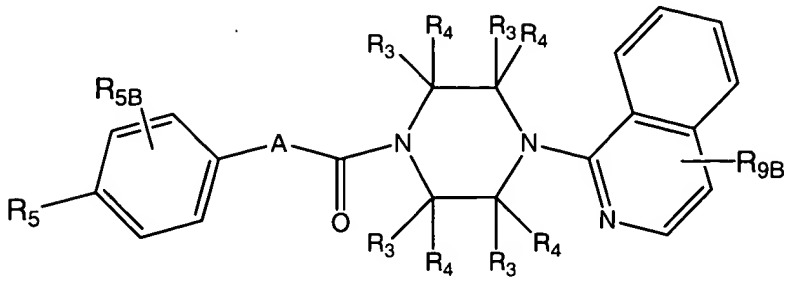
161. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and C_{1-6} alkyl;

R_3 and R_4 are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl);

R_5 is selected from the group consisting of halogen, halo(C_{1-6})alkyl, C_{3-6}alkyl substituted with 0-3 R_6, C_{2-6}alkenyl substituted with 0-3 R_6, (C_{3-8}cycloalkyl)C_{1-4}alkyl substituted with 0-3 R_6, and Y;

R_{5B} and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy;

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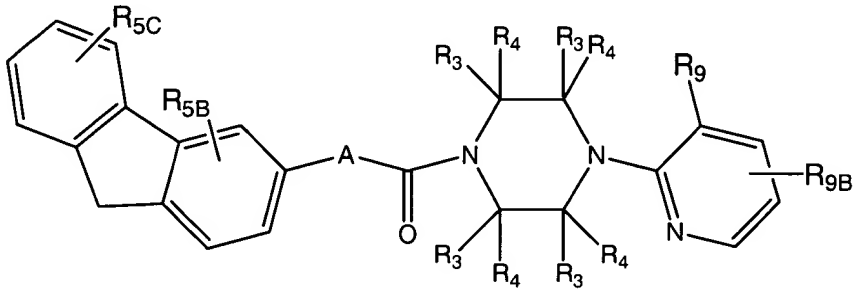
R_6 is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4}alkyl), [and] -N(C_{1-4}alkyl)(C_{1-4}alkyl) and Y;

Y is independently selected at each occurrence from C_{3-8} cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio.

169. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_BR_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen [or] and C_{1-6} alkyl;

R_3 and R_4 are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl);

R_{5B}, R_{5C}, and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy; and

R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-3})alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-3}alkyl)(C_{1-3}alkyl).

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